

CLAIMS

1. A method of treating a patient, comprising the step of delivering to the patient's cardiac autonomic structures nucleic acid which, when expressed, increases nitric oxide synthase levels.
2. The use of nucleic acid which, when expressed in cardiac autonomic structures, increases nitric oxide synthase levels, in the manufacture of a medicament.
3. The method or use of any preceding claim, for increasing cardiac vagal tone and/or responsiveness, for increasing bradycardia, for reducing cardiac autonomic impairment, for reducing the risk of sudden cardiac death, for reducing arrhythmia (*e.g.* atrial fibrillation and/or ventricular arrhythmia), for reducing the risk of myocardial infarction, and/or for reducing hypertension.
4. The method or use of any preceding claim, wherein nucleic acid is delivered to the vagus nerve.
5. The method or use of any preceding claim, wherein the nitric oxide synthase is NOS-1 and/or NOS-3.
6. The method or use of claim 5, wherein the NOS-1 is human NOS-1.
7. The method or use of any preceding claim, wherein the nucleic acid is targeted to cardiac tissue.
8. The method or use of any preceding claim, wherein expression of the nitric oxide synthase from the nucleic acid is regulated by a non-constitutive promoter.
9. The method or use of any one of claims 1 to 7, wherein expression of the nitric oxide synthase is regulated by a promoter which is specifically active in cholinergic ganglia tissue.
10. The method or use of any preceding claim, wherein the nucleic acid is packaged within a non-viral gene therapy vector.
11. The method or use of claim 10, wherein the nucleic acid is delivered as naked DNA.
12. The method or use of any preceding claim, wherein vagal tone in the patient is increased by at least 10%.
13. The method or use of any preceding claim, wherein the nucleic acid comprises DNA.
14. The method or use of any preceding claim, wherein the nucleic acid is non-replicating.
15. The method or use of any preceding claim, wherein the nucleic acid is non-integrating.
16. The method or use of any preceding claim, wherein the nucleic acid is an autonomously replicating episomal or extrachromosomal vector, such as a plasmid.

17. The method or use of any preceding claim, wherein the nucleic acid is delivered to the heart within microbubbles which can be disrupted by ultrasound.
18. A nucleic acid molecule comprising a non-constitutive promoter and a coding sequence, wherein:
5 (a) the promoter is operably linked to the coding sequence to control transcription of the coding sequence; (b) the promoter is specifically active in cholinergic ganglia tissue; and (c) the coding sequence encodes a nitric oxide synthase.
19. The nucleic acid of claim 18, for use as a medicament.